

Management of Gestational Diabetes Mellitus

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Gestational diabetes mellitus (GDM) is a frequent medical problem during pregnancy. It is associated with an increased risk of complications for GDM mother and the offspring. There is increasing evidence that GDM may increase the risk of future type 2 diabetes and cardiovascular disease in mothers, and may also increase the risk of obesity and diabetes in children. Therefore GDM affects health for a lifetime. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed a new screening approach for pre-diagnosed diabetes at the first prenatal visit and diagnostic criteria for GDM in accordance with perinatal outcomes. Nonetheless, controversies still exist about these issues. There is a positive linear association between increasing maternal glucose at oral glucose tolerance testing and risk of important perinatal outcomes. In managing the GDM patients, an individualized medical approach is essential. If maternal glucose levels have increased, insulin can be used to achieve glycemic targets. Postpartum screening for diagnosing of diabetes is essential for women with previous GDM.

Key words: gestational diabetes mellitus; diagnosis; management

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INTRODUCTION

Gestational diabetes mellitus is a common complication during pregnancy. Regardless of the time of the diagnosis, GDM has been defined as a key degree of glucose intolerance during pregnancy [1]. Recently, the American Diabetes Association (American Diabetes Association, ADA) clearly defined GDM as diabetes diagnosed in the second or third trimester of pregnancy [2]. Obesity increases in young women, and the age of women's gestation also increases. The prevalence of GDM has also increased. The prevalence of gestational diabetes mellitus was 8.0% based on the Korea National Health Insurance Claims Database [3]. Gestational diabetes mellitus is frequently associated with gestational hypertension, increased frequency of cesarean section, complications such as impaired delivery, and dysesthesia. In addition, the probability of overt

diabetes developing after delivery increases by seven fold compared to non-GDM patients [4]. For the offspring, the risk of large for gestational age (LGA), neonatal hypoglycemia, neonatal bone and nerve injuries are increased. In the long term, there is a higher risk of diabetes to occur in adolescence [5]. In view of increasing prevalence of GDM worldwide and its established association with adverse fetal, neonatal and their long term complications, we have to look into possible interventions for preventing and managing GDM.

DIAGNOSTIC CRITERIA FOR GESTATIONAL DIABETES MELLITUS

The screening and diagnostic criteria for gestational diabetes mellitus are conflicting. There is no unified standard tool worldwide. Controversies exist regarding selective screening

for high-risk patients only or general screening by all pregnant women (Universal screening), timing of screening, and one-step or two-step approach.

The diagnostic criteria for gestational diabetes with the 100 g oral glucose tolerance test was proposed in 1964 by O'Sullivan and Mahan [6]. Based on the mean of four whole blood glucose and standard deviation in 752 pregnant women, glucose levels over 2 SD (about 2%) confirmed the diagnostic criteria of GDM in the United States [6]. These criteria were chosen to diagnose postpartum diabetes in women. In 1982, Carpenter and Coustan revised this criteria more precisely [7].

However, there was increasing evidence that the degree of hyperglycemia was closely related to the occurrence of perinatal complications.

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study showed that the incidence of complications of perinatal and perinatal complications was found to be continuous in 25,000 pregnant women [8]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) suggested new criteria which increased the risk of newborn weight (> 90th percentile), cord blood C-peptide (> 90th percentile), body fat ratio (> 90th percentile) compared to the mean blood glucose group. A new diagnostic tool for gestational diabetes increases the risk by 1.75 times [9]. And that is, in the early stages of pregnancy, that recommend that the 75g oral glucose tolerance test be performed during 24 to 28 weeks of gestation in all pregnant women.

The ADA has been using the diagnostic criteria proposed by IADPSG since December 2010. But the American Congress of Obstetricians and Gynecologists (ACOG) continued to recommend a two-step approach. In 2013 World Health Organization (WHO) and the American Endocrinology Society accepted the IADPSG criteria [10,11]. However, the National Institute of Health (NIH) recommend a two step approach, because there are no intervention studies to improve pregnancy

outcomes and there is a significant economic burden [12]. And now, after 2014, ADA accepted the IADPSG diagnostic criteria and two-step approach [13] (Table 1).

SCREENING FOR GESTATIONAL DIABETES MELLITUS IN EARLY PREGNANCY

Diabetic women who are not diagnosed during pregnancy are at risk of congenital anomalies due to uncontrolled hyperglycemia. Most current guidelines are based on the first visit of pregnancy, especially in the high-risk group, recommending screening for the pregestational diabetes [9-11]. The criteria for diagnosing diabetes early in pregnancy are fasting plasma glucose \geq 126 mg/dL, random plasma glucose \geq 200 mg/dL, or HbA1c \geq 6.5%.

However, WHO does not include HbA1c in its diagnosis of diabetes [11]. In general, prior to 24 weeks of gestation, there is insufficient evidence to recommend treatment with gestational diabetes mellitus [14]. However, in the IADPSG, diabetes \geq 92 mg/dL was diagnosed as gestational diabetes [9].

MEDICAL MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

By diagnosing and managing gestational diabetes mellitus, perinatal complications (LGA and preeclampsia) of the population were decreased in two large randomized clinical trials [15,16]. Recently, in meta-analysis, they could reduce preeclampsia, LGA and shoulder dystocia, but neonatal hypoglycemia and future maternal metabolic abnormalities were not changed [17].

BLOOD GLUCOSE GOALS AND MONITORING

ADA suggested glycemic control as follows: pre-eclampsia \leq 95 mg/dL, 1 hour postprandial blood glucose \leq 140 mg/dL, and 2 hours postprandial blood glucose \leq 120 mg/dL [13,18]. The goals of ADA presented are not based on randomized clinical trials, it came from expert opinions. Therefore, we have to research about what's the optimal target of maternal glucose levels.

GDM patients usually check their blood glucose levels four to seven times a day (fasting and three postprandial 1~2 hours). There have been reports that postprandial blood glucose is more effective in decreasing the neonatal outcomes than fasting

Table 1. Diagnostic criteria for gestational diabetes mellitus

	100 gram OGTT (after 50 gram OGTT) Carpenter-Coustan [7]	75 gram OGTT IADPSG [9]
Fasting (mg/dL)	95	92
1 hour (mg/dL)	180	180
2 hour (mg/dL)	155	7 DEF
3 hour (mg/dL)	140	153

OGTT, oral glucose tolerance test; IADPSG, The International of Diabetes and Pregnancy Study Groups

blood glucose [19].

LIFESTYLE INTERVENTIONS

Clinical nutrition is the basis of gestational diabetes management. All Diabetes mellitus patients should be educated by experienced clinical dieticians. Clinical nutrition therapy of gestational diabetes mellitus offers appropriate meal plans that provide carbohydrates to prevent ketogenesis. The meal plans should be individualized, based on nutritional assessment per patient which considers factors such as pre-pregnancy weight, level of physical activity, and weight gain during pregnancy.

In the obese mother, calorie-restriction has been suggested as a useful method for controlling blood glucose, but limitations in caloric intake can cause ketosis. Excessive caloric restriction can have a negative effect during pregnancy. To adequately control postprandial blood glucose, a water-restricted diet (50% in Korea) is recommended. Three meals and two to three snacks distributed throughout the day is recommended.

Regular exercise can improve blood glucose levels. So GDM patients are recommended to exercise

regularly. Cardiovascular effect of exercise can lower blood glucose and avoid unnecessary insulin

therapy. It takes 20 to 30 minutes of exercise time to effectively lower blood glucose. However,

exercise should be avoided during pregnancy, if patients have hypertension, premature rupture of

amniotic membrane, delayed fetal growth, history of preterm delivery, persistent bleeding, and

cervical incompetence.

PHARMACEUTICAL INTERVENTIONS

Insulin can control maternal hyperglycemia even if they did extensive lifestyle therapy during pregnancy. Medical nutritional therapy and exercise should be performed at least 1 to 2 weeks. If blood glucose couldn't be controlled, doctors have to start insulin therapy. If maternal blood glucose level is well controlled, fast fetal growth with respect to gestational age require insulin therapy [20]. In pregnancy, various insulin preparations that can be used include fast-acting insulin analogs (Lispro, aspart), human insulin (RI, NPH), and long acting insulin analogs (detemir). Insulin glargine (Glargine) is not allowed due to lack of randomized clinical trial data [10]. And insulin treatment should be adjusted to individual needs.

Over the past 30 years, insulin has been used in the medical treatment of gestational diabetes as 1st choice medication. However, the use of oral hypoglycemic agents increased in the recent 10 to 20 years. Metformin and glibenclamide are evaluated for insulin alternatives. In metformin-treated studies, equivalent pregnancy outcomes were shown, such as decreased weight gain and maternal hypoglycemia [21]. However, in a Metformin in Gestational Diabetes (MIG) study, 46.3% of the metformin group required insulin treatment [22]. ADA recommends insulin treatment for GDM, while ACOG recommends metformin or glyburide in addition to insulin [23,24]. However, there is no long-term clinical data in the offspring exposed to oral medication in the prenatal period. So insulin treatment is recommended to control hyperglycemia of GDM.

MEDICAL MANAGEMENT AFTER DELIVERY

Women with gestational diabetes mellitus usually have normal blood glucose after delivery. But overt diabetes can develop over time [4]. Therefore, women with gestational diabetes mellitus are considered a high-risk group. Therefore, postpartum diabetes education and lifestyle modifications are important to prevent diabetes mellitus.

There is still controversy about the timing and methods to detect diabetes after delivery. The ADA and Endocrinology Society reported that postpartum 75 gram oral glucose tolerance test is recommended at six to 12 weeks [10,13,23]. Moreover, screening of diabetes should be done every one to three years afterwards [13]. Currently, we can use HbA1C, fasting plasma glucose, and 75 g oral glucose tolerance test to assess glucose abnormality. Aggressive lifestyle modification therapy such as regular exercise can prevent or delay the development of diabetes after GDM [25].

CONCLUSION

All pregnant women should be recommended to be screened for diabetes mellitus. The IADPSG diagnostic criteria were the first criterion based on perinatal complications of GDM. Controversies over whether to apply this criterion globally are still ongoing and the issue is a hot topic for management of GDM. For this, we need nationwide clinical trials to be established for diagnostic criteria of GDM for the Korean population. The treatment of GDM through clinical nutrition

and exercise therapy must be a priority. Insulin is the primary treatment choice when blood glucose is not controlled. Women who have been diagnosed with GDM should be screened for diabetes on a regular interval. And precise mechanism about the development of GDM, and postpartum diabetes mellitus should be consistently researched and studied.

REFERENCES

- Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997;20:1183-97.
- American Diabetes A. 2. Classification and Diagnosis of Diabetes. *Diabetes Care* 2017;40:S11-S24.
- Son KH, Lim NK, Lee JW, Cho MC, Park HY. Comparison of maternal morbidity and medical costs during pregnancy and delivery between patients with gestational diabetes and patients with pre-existing diabetes. *Diabet Med* 2015;32:477-86.
- Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet* 2009;373:1773-9.
- Nehring I, Chmitorz A, Reulen H, von Kries R, Ensenaer R. Gestational diabetes predicts the risk of childhood overweight and abdominal circumference independent of maternal obesity. *Diabet Med* 2013;30:1449-56.
- O'Sullivan JB, Mahan CM. Criteria for the Oral Glucose Tolerance Test in Pregnancy. *Diabetes* 1964;13:278-85.
- Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol* 1982;144:768-73.
- Group HSCR, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991-2002.
- International Association of D, Pregnancy Study Groups Consensus P, Metzger BE, Gabbe SG, Persson B, Buchanan TA, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676-82.
- Blumer I, Hadar E, Hadden DR, Jovanovic L, Mestman JH, Murad MH, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2013;98:4227-49.
- InDiagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy. Geneva; 2013.
- National Institutes of Health consensus development conference statement: diagnosing gestational diabetes mellitus, March 4-6, 2013. *Obstet Gynecol* 2013;122:358-69.
- American Diabetes A. 2. Classification and Diagnosis of Diabetes. *Diabetes Care* 2016;39 Suppl 1:S13-22.
- Moyer VA, Force USPST. Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2014;160:414-20.
- Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005;352:2477-86.
- Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009;361:1339-48.
- Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Donovan L. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. *Ann Intern Med* 2013;159:123-9.
- American Diabetes A. Gestational diabetes mellitus. *Diabetes Care* 2003;26 Suppl 1:S103-5.
- de Veciana M, Major CA, Morgan MA, Asrat T, Toohey JS, Lien JM, et al. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. *N Engl J Med* 1995;333:1237-41.
- Kjos SL, Schaefer-Graf U, Sardesi S, Peters RK, Buley A, Xiang AH, et al. A randomized controlled trial using glycemic plus fetal ultrasound parameters versus glycemic parameters to determine insulin therapy in gestational diabetes with fasting hyperglycemia. *Diabetes Care* 2001;24:1904-10.
- Gui J, Liu Q, Feng L. Metformin vs insulin in the management of gestational diabetes: a meta-analysis. *PLoS One* 2013;8:e64585.
- Rowan JA, Hague WM, Gao W, Battin MR, Moore MP, Mi GTI. Metformin versus insulin for the treatment of gestational diabetes. *N Engl J Med* 2008;358:2003-15.
- American Diabetes A. Standards of medical care in diabetes--2014. *Diabetes Care* 2014;37 Suppl 1:S14-80.
- Committee on Practice B-O. Practice Bulletin No. 137: Gestational diabetes mellitus. *Obstet Gynecol* 2013;122:406-16.
- Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, et al. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *J Clin Endocrinol Metab* 2008;93:4774-9.